SUMMARY OF DATA FOR CHEMICAL SELECTION

CELLULOSE INSULATION

NOMINATION HISTORY

Nomination Source:	Dr. E. E. McConnell
Date of Nomination:	July 1994
Recommendations:	In-depth toxicological evaluation including long-term inhalation bioassay
Rationale/Comments:	_ Potential for widespread human exposure _ Proposed as "safe" alternative to asbestos for use in production of asbestos cement pipe and household/industrial insulation _ Lack of data on potential carcinogenic activity of cellulose insulation

Prepared for NTP by Technical Resources International, Inc., under Contract No. NO1-CP-56019 (7/95)

SUBSTANCE IDENTIFICATION

Cellulose insulation (CI) is a type of thermal insulation consisting of recycled newspapers treated with fire retardant chemicals. There is no information on fiber size of the cellulosic material in the final product.

Technical Products and Impurities: CI may contain fire retardant chemicals, most often boric acid, borax or ammonium sulfate; buffers such as gypsum; residuals of the paper production process (e.g., sodium hydroxide, sodium sulfide, formaldehyde, chlorine, fluorine, lead, iron, sulfur compounds); and remnants of dyes, resins, gums, talc, printing inks, and various solvents (Davis, 1993; Lea, 1995).

Performance Standards

In 1978, the Consumer Product Safety Commission (CPSC) issued performance standards to ensure the safety of CI. These standards required that all CI produced after September 7, 1978, must pass flammability and corrosiveness tests specified in General Services Administration (GSA) standard HH-I-515-C that mandates performance of CI products purchased by government agencies. Under the CPSC standards, CI must have a flame spread rating of from 0 to 25 when placed in a 25-foot Steiner tunnel and ignited. In addition, the insulation must pass a corrosiveness test since some chemical treatments used to reduce cellulose flammability can corrode metal and undermine a building's structural integrity (Anon., 1978a). These standards were amended in October, 1979 to reflect the newer version of the federal standard HH-I-515-D, to tighten flammability and corrosion standards and mandate updated labeling. The amended standard requires a critical radiant flux test on samples, instead of tests in a Steiner tunnel; replaces the blown-density test methods employed with cyclone shaker tests; requires more exacting procedures for determining the corrosiveness of the samples; and requires that labels state that the product meets the amended law. The amendment also requires all flammability test specimens to have a critical radiant flux $\geq$0.12 watt/cm^2 and bans the use of any CI tested that causes perforations in copper, aluminum, or steel coupons in a 14-day corrosion test. (Anon., 1979a). The CPSC standard, although it does not encompass as many tests as the GSA standard, is mandatory for all manufacturers (Chrenka, 1980).

There are two standard specifications issued by the American Society for Testing and Materials (ASTM) pertaining to CI. ASTM C 739-91 covers the composition and physical requirements of chemically treated, recycled cellulosic fiber (wood-base) loose-fill type thermal insulation for use in attics or enclosed spaces in housing and other framed buildings within the ambient temperature range from -45.6 to 82.2°C (-50 to 180°F) by pneumatic or pouring application. ASTM C 1149-90 covers the physical properties of self-supported spray applied cellulosic fibers intended for use as thermal or acoustical insulation, or both, and covers chemically treated cellulosic materials intended for pneumatic applications where temperatures do not exceed 82.2°C (180°F) and where temperatures will routinely remain below 65.6°C (150°F). Both standards address density, thermal resistance, smoldering combustion, fungal resistance, corrosion, moisture vapor absorption, and odor. In addition, ASTM C 739-91 for loose-fill thermal insulation addresses average critical radiant flux and starch content, and ASTM C 1149-90 for spray-applied cellulosic insulation addresses surface burning characteristics, adhesive/cohesive strength, flame resistance permanency, substrate deflection, and air erosion (ASTM, 1994a,b).

EXPOSURE INFORMATION

Production and Producers: CI is manufactured from cellulosic materials which are commonly combined with inorganic fire retardant chemicals. The cellulosic material generally derives from recycled newspapers and, sometimes, from other uncoated paper products and wood chips. Coated paper or fine paper are best avoided since coatings or smooth surface textures resist the addition of fire retardant chemicals (Zicherman & Fisher, 1978; Chrenka, 1980; Barton *et al*., 1981; McConnell, 1994).

In the 1970's, manufacture of CI used the hammermill technology to produce insulation of a density of about 2 lbs/ft^3 or more . In a typical hammermill operation, raw materials were first sorted and then conveyed into mills that pre-shredded and pulverized the materials into a fibrous, reasonably homogeneous bulk material. In the shredder, which had either fixed or swinging rotary hammers, material was forced out through a millscreen with approximately 3 inch openings. The shredded paper was then pneumatically moved to an intermediate mill where it was forced through a smaller millscreen. After leaving the intermediate mill, the material was fed to a holding bin which was used to achieve a uniform feed rate to the next, or final, mill. In the final mill, the material was forced through a millscreen of about _ inch openings and chemicals with fire retardant properties, typically boric acid, borax, and alumina trihydrate, were introduced simultaneously at 20 to 25% loading with the ground paper to achieve flame retardancy. Prior to adding the chemicals at this stage, they were blended, proportioned, and finely ground to the consistency of flour in order to disperse into the fiber more readily. In the final stage of the process, the finished product was conveyed to a bagging unit for packaging and to a dust collector (Zicherman & Fisher, 1978; Chrenka, 1980; Lea, 1995).

Today, manufacture of CI uses rotating disks (light density mill, AFT ringer, or Haybuster), similar to a salad shooter, to produce a light-density product of about 1.5-1.8 lbs/ft^3. This method does not crush the fibers as much, bringing it back to the pulp state (Lea, 1995).

The leading brand, Louisiana Pacific's Nature Guard, is manufactured primarily from recycled newspaper that is treated with borax and boric acid. Other cellulose brands, like Suncoast's U.S. Fiber, are similarly produced from old newspapers (Sinanoglu, 1994).

A US company has also patented a method of making fire-resistant CI consisting of a finely divided cellulose mixed with talc (5-25% by weight) and the optional addition of boron compounds (up to 10% by weight) and other additives (Bird *et al*., 1980). According to the Cellulose Insulation Manufacturing Association, talc is not currently used in the manufacture of CI (Lea, 1995).

The manufacture of cellulose-reinforced cement board used as a replacement for gypsum board or asbestos-based insulation materials has been made easier by the development of a layer "former" that replaces conventional sieves (Anon., 1980a).

Prior to the mid-1970's, there were roughly 100 firms manufacturing CI. Between 1975-1976 the demand for insulation heightened due to new energy efficiency awareness, and a surge of companies began producing CI. By the end of 1977, there were approximately 950 manufacturers. Many of these new manufacturers had no knowledge of acceptable manufacturing processes and produced inferior and unsafe insulation. Inferior products as well as incorrect installation of CI around recessed lights or other heating products resulted in many home fires where the first material ignited was the CI. Another major problem was the collapse of metal buildings corroded by CI containing ammonium sulfate. Consequently, in 1978, the CPSC imposed mandatory standards for flammability and corrosion of CI which were updated in 1979. Establishment of federal regulations governing the manufacture of CI and adverse publicity regarding flammability and corrosiveness of some CI caused many firms to abandon the business. The number of CI manufacturers dropped to less than 450 firms operating in 1978, less than 200 in 1980, and 169 in 1983 (Anon., 1980b, 1984; Chrenka, 1980). In 1991, it was estimated that there were about 100 manufacturers of CI (Anon., 1991a).

The Cellulose Insulation Manufacturers' Association estimates that there are approximately 50 companies that presently manufacture CI (Lea, 1995). The Thomas Register lists the following companies as CI manufacturers (Dialog Information Services, 1995).

Ahpla, Inc.
Orange Park, FL

All Weather Insulation Co., Inc.
Springfield, KY

American Cellulose Mfg., Inc.
Minonk, IL

Cellulose Insulation Mfg., Inc.
Midvale, UT

Central Fiber Corp.
Wellsville, KS
Champion Insulation, Inc.
Lomira, WI

Eagle Lake Industries
Lindale, TX

Energy Zone Mfg.
Buffalo, MN

Four Seasons Insulation Mfg. Co.
Charleston, IL

Hamilton, Mfg., Inc.
Twin Falls, ID
Incide Technologies, Inc.
Phoenix, AZ

Midwest Thermal Products
Oklahoma City, OK

National Fiber, Inc.
Belchertown, MA

Nu-Wool Co., Inc.
Jenison, MI

Polar-Therm Insulation Co.
Cape Girardeau, MO

Pro Star
Coatesville,IN

Solar Therm Mfg. Co., Inc.
Marshall, TX

Springer, Barry N., Inc.
Sabattus, ME

Suncoast Insulation Mfg. Co.
Tampa, FL

Tascon, Inc.
Houston, TX

Thermoguard Co.
Billings, MT

Western Fibers, Inc.
HollisOK

Other manufacturers of CI include Cell-Pak, Louisiana-Pacific Corp., and Greenstone Industries. Cell-Pak (Decatur, AL) has a 40-person plant that consumes about 6.5 thousand tons per year of newspapers and has an output capacity of 2,500 bags/day of CI (Anon., 1991a). Louisiana-Pacific Corp, opened a CI plant in Savage, MD in 1992 that uses about 30 thousand tons per year of recycled newspaper. The company has similar facilities in Missouri and Ohio (Anon., 1991b, 1992). GreenStone Industries, Inc., the only publicly owned CI company in the US, has plants in several states, including Nebraska, Arizona, Oregon, Virginia, Georgia, and Indiana. Market analysts project that GreenStone Industries, Inc. will continue to grow as CI replaces fiberglass (Anon., 1994a,b, 1995).

Production levels are difficult to obtain as many of the producers of the material are small enterprises. The estimated production capacity of cellulose loose-fill insulation was 2.4 million tons in 1980 (Neisel & Verschoor, 1981). According to an industry survey, CI manufacturing sales fell from $39.4 million in 1982 to $36.3 in 1983 as production declined from 689 thousand tons to 634 thousand tons (Anon., 1984). The best available data indicate that production of CI is presently somewhere between 270 and 420 thousand tons (McConnell, 1994).

The manufacture of CI accounted for 14% of consumption of waste newspapers in 1977 and 24% in 1980 (Barton *et al*., 1981). Estimated consumption of old newspaper by CI manufacturers in 1979 was about 646 thousand tons (Anon., 1980a).

A report on the markets for waste newspaper in four south Atlantic states found that CI producers in Georgia consumed 78.2 thousand tons of newspapers in 1980 compared with a combined 18.3 thousand tons in North Carolina and South Carolina and 14.7 thousand tons in Florida (Barton *et al*., 1981).

Consumption of three chemicals used as fire retardants during peak production of cellulosic insulation in the mid-1970's is presented in Table 1.

Table 1. US consumption of 3 chemicals as fire retardants in cellulosic insulation

Chemical	1976 (thousand tons)	1977 (thousand tons)
Boric acid	20.6	45.3
Boron	5.5	18.3
Boric oxide	17.7	58

Source: Anon. (1978b)

Use Pattern: Although patents for cellulosic fiber insulation were issued in the 1800's, the product did not find a firm foundation in the marketplace until the 1950's. Since that time it has been one of the principal thermal insulations used in retrofitting (i.e., addition of thermal insulation) of private homes and small, multiple dwelling units and, to a limited extent, in new construction of buildings. The utility of CI is based on the ability of cellulose to entrap air both between fibers and within fibers; this interweaving of strands of fibers, entrapping millions of air pockets, provides the excellent insulating quality of defibered cellulose. CI is more economical than other thermal insulation partly because it is more efficient. In addition, it reaches more areas than other insulation materials because of the application process (Anon., 1977; Zicherman & Fisher, 1978; Chrenka, 1980; Sinanoglu, 1994).

The most common method of installing CI is to blow it into new or existing structures. It is normally applied by an open blowing process into attics but is also installed by a closed blowing process into sidewalls in retrofit situations. It can also be applied by hand, such as pouring the insulation out of a bag between and over attic joists. Contractors also install these materials into existing exterior walls by drilling holes in siding materials between wall studs and blowing the insulation into wall cavities (Anon., 1977; Zicherman & Fisher, 1978; Davis, 1993; McConnell, 1994). In addition, CI can be applied with a spray gun. In this type of application, shredded newspaper is mixed with a water-based adhesive and then sprayed onto walls or ceilings. This method has been used to cover and protect against existing asbestos-containing insulation (Cohn, 1981). Spray-applied CI can be installed on complex surfaces and substrates (e.g., barrel vaults, corrugated decks, concrete "T" or pans, flat surfaces, wood, concrete, metal, sheetrock, plaster) and can be used in both new construction and renovation. The thickness of the finished product can be altered to provide different levels of thermal or acoustical performance (Anon., 1990).

A NIOSH investigation described the application of CI by a community program for home weatherization for low income residents. A minimum of two employees was required. One employee dumped bags of cellulose into a hopper located off the rear of a weatherization truck, and a motor at the bottom of the hopper blew the insulation material through a long hose to its point of application. Its flow and distribution were controlled by a second employee through the use of a regulator on the end of a hose. The cellulose is generally distributed directly between the rafters of attics or into holes drilled in the outside walls of the residences (Daniels *et al*., 1985).

CI has also been proposed as a product that is "safer" than fibrous glass insulation and as a substitute for asbestos in cement products (McConnell, 1994; Davis, 1993).

CI shipments between 1969 and 1976 are shown in Table 2.

Table 2. Cellulosic Insulation Shipments 1969-1976

Year	Quantity (thousand tons)
1969	100
1970	110
1971	125
1972	145

1973	190
1974	175
1975	210
1976	300

Source: ICF, Inc. (1977)

CI accounted for 20% of the entire building insulation market in 1975, 20-25% in 1978, and 15-20% shortly afterwards. Relative demand in 1975 for CI was 10% for industrial equipment and pipes and 90% for building construction [10% for new residential construction, 75% for reinsulation/remodelling, and 5% for commercial/industrial construction (ICF, Inc., 1977; Anon., 1981; Barton *et al*., 1981)]. In 1979, the CI brand Shelter Shield, manufactured by Diversified Insulation in the United Kingdom, accounted for 40% of the US insulation market (Anon., 1979b).

Demand for CI has declined since the 1970's. In 1991, it accounted for 10% of the insulation market for single-family residential homes (Anon., 1991a). CI accounted for about 10% of the insulation market in 1993 and is projected to remain at this level in 1998. Demand was estimated to be 265.5 thousand tons in 1993 and is projected to be 292.5 thousand tons in 1998, indicating 2% growth per year (The Freedonia Group, Inc., 1994).

Between 1975-1980, one in eight homeowners insulated their homes with CI. During this same period, federally funded weatherization programs that insulate homes of low-income families also used CI almost exclusively (Chrenka, 1980). A survey by the Consumer Product Safety Commission in 1978 estimated that 3 million houses had CI installed between January 1976 and September 1978 (Levin & Purdom, 1983).

<u>Human Exposure</u>: The number of workers exposed to CI is unknown. The National Occupational Exposure Survey (NOES) which was conducted by the National Institute for Occupational Safety and Health (NIOSH) between 1981 and 1983 does not contain information on CI. Several NIOSH investigations and a German study have documented occupational exposure to CI.

A 1984 NIOSH investigation of health problems among personnel working with various insulating materials used for weatherization of homes found that concentrations of total particulate exceeded the ACGIH-recommended threshold limit value and the OSHA permissible exposure limit. The bulk of the material composing the CI would be considered to be nuisance dust. The highest concentrations were present in personal samples collected during the blowing of cellulose into attic areas, with 8-hour time-weighted averages of 20.8 and 34.5 mg/m^3 found at the two different sites monitored. Concentrations were significantly lower when blowing insulation in outside walls (5.2 mg/m^3) and during the loading of the hopper off the back of the weatherization truck (5.2 and 4.3 mg/m^3). The NIOSH investigators noted that all personnel working at these activities were wearing NIOSH/MSHA approved respiratory protection, which if properly used and fitted, should have greatly reduced the actual exposure (Daniels *et al*., 1985).

A 1990 NIOSH evaluation of asbestos exposure during low-income housing weatherization procedures documented high levels of dusts and cellulose fibers associated with CI installation. These short-term exposures included levels of 2.2-4.6 mg/m^3 for workers blowing insulation in holes in walls, 13.4 mg/m^3 for a worker feeding bags of CI into the blower hopper, and >40.8 mg/m^3 for a worker blowing insulation inside an attic. The investigators noted that company policy required workers to wear a half-face respirator with a combination HEPA/organic vapor cartridge when spraying CI or when entering an attic, a crawl space, or knee wall (McCammon & Lee, 1990; Tharr, 1991). Therefore, workers adhering to respirator policy should have minimal respiratory exposure to cellulose fibers.

A German study investigated fibrous dust emission from CI (Isofloc) during installation and use. In all measurements, a large increase in fiber and dust exposure was noted with increasing time of exposure during installation. The tests were conducted primarily during the beginning of the installation phase and up to 2.5 hours into the installation phase. Table 3 presents the findings of these tests. During insulation of a wooden floor, the German threshold limit for respirable dust of 6 mg/m^3 was exceeded. The investigators noted that the manufacturer of the insulation permits the installation of its products only by specialty firms and encourages them to use masks and respirators (Tiesler & Schnittger, 1992). A response to the investigation further pointed out that the CI investigated in the study is used primarily in the interior of airtight hollow spaces. In addition, the technical information and training provided to the installers for the production of these airtight layers further precludes any dust exposure to the occupants (Welteke, 1993).

No quantitative information was found on consumer exposure to CI.

Environmental Occurrence: A study on emissions of organic compounds from building materials determined that CI had relatively few emissions. No specific details were provided in the study (Tsuchiya, 1986). An article on the need for standardized testing procedures for all products capable of liberating respirable fibers reported the results of an unpublished study on the liberation of respirable fibers from a series of cellulose products subjected to mechanical disruption. All products liberated respirable fibers, typically in the range of 1-4 fibers/ml. One cellulose product liberated 18 fibers/ml (Davis, 1993).

Table 3. Findings of a German study on fibrous dust emission from cellulose insulating materials during installation and use

Scenario	Respirable Dust (mg/m^3)			Respirable Particles (million fibers/m^3)					
				<1 µm diameter			< 3 µm diameter		
	Average	Median	Maximum	Average	Median	Maximum	Average	Median	Maximum
Insulation of a wooden floor	9.5	7.9	19.7	9.3	12.4	17.6	32.1	42.3	57.3
Blowing-in into a sloped pitch roof	2.6	-	2.9	3.9	-	4.0	12.2	-	12.2

(Tiesler & Schnitteger, 1992)

Regulatory Status: The OSHA (1994a,b) permissible exposure limit (PEL) for general industry as well as for the construction industry is 15 mg/m^3 for total dust and 5 mg/m^3 for the respirable fraction averaged over an eight-hour work shift.

The ACGIH has recommended a threshold limit value time-weighted average (TLV-TWA) of 10 mg/m^3 for cellulose dust (ACGIH, 1994).

The NIOSH recommended exposure limit (REL) for cellulose is 5 mg/m^3 for the respirable fraction and 10 mg/m^3 for total dust averaged over a ten-hour work shift (NIOSH, 1992).

EVIDENCE FOR POSSIBLE CARCINOGENIC ACTIVITY

Human Data: No epidemiological studies or case reports investigating the association of exposures to CI and cancer risk in humans were identified in the published literature. Although the direct effects of CI on human health have not been studied, cellulose particles from other sources have been associated with the formation of foreign body granulomas in humans.

Zeltner and coworkers (1982) reported a case of fatal pulmonary granulomatosis in a male drug abuser from illicit intravenous injections of microcrystalline cellulose, a binding agent in pentazocine tablets. Histopathological examination showed extensive foreign body granulomas in the lumena and walls of pulmonary vessels and in the pulmonary interstitium. The granulomas consisted of macrophages and foreign body giant cells and often had a rim of small lymphocytes and a few plasma cells. Neutrophils were almost absent. The granulomas contained gray to green, birefringent, needle- or rod-shaped crystals with the histochemical properties of microcrystalline cellulose. Pulmonary foreign body granulomatosis in a male drug abuser as a result of intravenous abuse of pentazocine was also reported by Fitzer (1987). The author noted that microcrystalline cellulose causes both embolic angiothrombosis and granuloma formation, that the granulomas may be primarily vascular and perivascular or interstitial, and that the interstitial lesions generally lead to pulmonary fibrosis.

In addition to intravenous injection, inhalation of drugs containing cellulose filler may also cause damage to the lungs. Fiberoptic transbronchial lung biopsy specimens from a male cocaine sniffer showed foreign body granulomas containing numerous birefringent needle shaped particles measuring up to 120 µm in length. Subsequent investigation confirmed cellulose as the causative agent (Cooper *et al*., 1983).

There have also been reports of granulomas occurring postoperatively in patients exposed to cellulose fibers during surgery. Possible sources of cellulose contamination in the operating theater include woven fabrics (cotton gowns, towels, and swabs) and non-woven materials (disposable drapes, masks, and hats). Brittan and coworkers (1984) described a case of cellulose granulomatous peritonitis in a 55-year-old woman which they ascribed to cellulose contamination during a previous surgery. Histological examination of nodules showed dense fibrovascular tissue in which numerous necrotizing tuberculoid granulomata were seen. The granulomata consisted of a wall of epithelioid histocytes enclosing either caseous material or masses of disintegrating nuclei. There were many multinucleate giant cells surrounding the central necrosis. Within the giant cells and necrotic debris, there were numerous hollow fibers of varying length with the characteristic morphological features of vegetable cellulose fibers. Three cases of cerebral granuloma were described by Ito and coworkers (1989). In each case oxidized cellulose had been used and left in place for hemostasis during craniotomies which took place 13 to 21 months previously. All of the granulomas consisted of mononuclear phagocytic and multi-nuclear giant cells and contained remnants of oxidized cellulose.

Animal Data: No 2-year carcinogenicity studies of CI in animals were identified in the published literature. Toxicity information on CI was limited to one subacute inhalation study in rats. Several studies have examined the toxic effects of cellulose dust and cellulose implants.

Cellulose Insulation: In an evaluation of the potential effects of dusts from CI, male and female SPF Wistar rats (number not reported) were exposed nose-only to 0, 0.1, 0.5, and 2.0 mg/l CI for 6 hours/day, 5 days/week for a total of 21 exposures. CI was purchased commercially and ground to produce a particulate of which 35 to 40% was potentially respirable by rats. The pulmonary pathology showed evidence of dose related changes in severity of the pulmonary response characterized by diffuse macrophage infiltration, microgranuloma formation, alveolitis, and epithelial hyperplasia. Limited collagen deposition was noted in the peribronchiolar interstitium at the high dose level (Hadley *et al*., 1992). McConnell (1994) reviewed the lung pathology from this study and noted that the inflammatory reaction (severe macrophage and granuloma formation) was more intense than that he had observed with chrysotile asbestos after 90-days exposure. He commented that foreign bodies of plant origin are typically highly antigenic and stimulate profound foreign-body reaction. He also suspected early collagen deposition and noted that normally it takes longer than 28 days for well developed fibrosis to be evident.

Cellulose Dust: In order to examine the ability of cotton dust to produce emphysema in an animal model, 8 to 9 male Syrian hamsters were administered intratracheal instillations of 0.75 mg/ 100 g/animal of respirable cotton dust twice a week for 6 weeks followed by an eight-week recovery period. Another group received 0.75 mg/100 g/animal of cellulose dust on the same schedule. The cellulose dust was microgranular cellulose, a thin-layer chromatography adsorbent produced from cotton fiber and provided as a powder. The mass median aerodynamic diameters of the cotton and cellulose dusts were 4.2 and 4.8 µm, respectively. Cotton dust instillation produced both granulomata and mild centrilobular emphysema. The cellulose-treated animals had decreased lung distensibility, noncaseating granulomata, and increased volume density of parenchymal tissue elements. These changes were cited as hallmarks of the histologically apparent lung fibrosis. The fibrotic response to cellulose occurred at a high lung burden (total dose was approximately 3 mg/g lung). The authors noted that the accumulation of particles and toxicity may have been due to overload of the lung's capacity to remove insoluble foreign material as well as any intrinsic toxicity of cellulose. They theorized that, in most environments, inhaled cellulose particle size may be too large for a significant parenchymal dose to accumulate which would account for the absence of reports of pulmonary fibrosis in response to environmental cellulose exposure (Milton *et al*., 1990).

The effects of a single intratracheal dose of cellulose dust, paprika dust, or paprika dust extract on the lungs of male CFY rats (5 animals per group) were determined 1 and 3 months after treatment. The 15 mg per animal dose of both cellulose dust and paprika dust resulted in alveobronchiolitis at the end of the first month and fibrotic changes at the end of the third month. As the extract of paprika dust caused no histopathological alterations, it was assumed that the high cellulose content of paprika was responsible for the histological reactions. The cellulose dust (Cellulosepulver MN 300 for thin layer chromatography) and paprika dust were suspended in physiological saline for dosing (Tatrai & Ungvary, 1992).

Tatrai and coworkers (1995) examined the role of cellulose in wood dust-induced fibrosing alveobronchiolitis. Male Sprague-Dawley rats (5 animals per group) were given single intratracheal doses of 15 mg germ-free respirable pine wood dust, cellulose (Cellulosepulver MN 300 for thin layer chromatography), fiber-free pinewood extract or saline. After 1 week or 1 month, the wood dust and cellulose induced morphologically identical granulomatous inflammation and fibrosis, whereas the fiber-free extract of wood dust did not cause pathological changes in the lungs. The authors had hypothesized that, since mammals have no enzyme for the digestion of ß-glycoside bonds in cellulose, cellulose may in part be responsible for the pulmonary toxicity of plant dusts. The authors also stated their plans to study the long-term biological effect of cellulose.

As part of a study to assess pulmonary reactions to inhaled cotton dust, four male guinea pigs were exposed to respirable particles of cellulose (Whatman microgranular cellulose powder CC41) for 6 hours for a single day. Chamber concentrations of cellulose dust ranged from 19.2 to 22 mg/m^3 and particle size (aerodynamic mass median diameter) ranged from 2.9 to 3 µm. Based on measurements of respiratory frequency and respiratory pattern during exposure as well as by pulmonary response to 10% CO_2 challenges before and after exposure, no response resulted from inhalation of cellulose powder (Ellakkani *et al*., 1984).

Cellulose Implants: Subcutaneous implants of 10x20x0.3 mm sheets of cellulose did not induce tumors in 12 female Fischer rats after 741 days. The other materials tested (silicone, polyvinylchloride, zirconia and an alkyl-a-cyanoacrylate) induced malignant fibrous histiocytoma (Hatanaka *et al*., 1993).

The inflammatory response in rabbit eyes was studied following implantation of 1 mm square pieces of cotton, cellulose or collagen into the anterior chamber and vitreous. In general, cotton was the least reactive, with collagen and cellulose moderately reactive. Cellulose was associated with progressive inflammation and marked granulomatous response (Peiffer *et al*., 1983).

Short-Term Tests: No mutagenicity or other genotoxicity studies of CI were identified in the published literature.

Cellulose Fibers: Schmitt and coworkers (1991) found that Cellulon fiber which is produced by a bacterial fermentation process employing a strain of *Acetobacter aceti xylinum* and most closely resembles powdered and microcrystalline cellulose, exhibited no genotoxic potential in four assays. At 66.7 - 2500 µg/plate, Cellulon did not cause increases in histidine revertants in *Salmonella typhimurium* strains TA98, TA100, TA1537 or TA1538 both with and without metabolic activation. Cellulon was negative for inducing chromosomal aberrations in Chinese hamster ovary (CHO) cells at 1990 - 8000 µg/ml both with and without metabolic activation. At 501 - 5010 µg/ml Cellulon was inactive in the *in vitro* rat primary hepatocyte UDS assay. Cellulon fiber was negative for inducing forward mutations at the HGPRT locus in CHO cells at 0.25 - 5 mg/ml both with and without metabolic activation.

Metabolism: No information on the metabolism of CI was identified in the published literature.

Cellulose is a major constituent of many foods of plant origin. As such it is a significant portion of the diet, but is neither degraded nor absorbed (FASEB, 1973).

Other Biological Effects: In a comparative study of the *in vitro* effect of various dusts on plasminogen activator (PA) production by mouse peritoneal macrophages, cellulose fibers were more active inducers of PA than chrysotile A and crocidolite (10 µg of these materials were enough to degrade 40% of the fibrin in less than 3 - 4 days). However, the authors noted that the study results showed no close correlation between known pathogenicity and *in vitro* fibrinolysis (Godelaine & Beaujay, 1989).

Human leukocytes were preincubated at 37˚C for 30 minutes with 0 - 100 µg/ml cellulose and the production of singlet oxygen and H_20_2 was related to the enhancement of light emission using Luminol. Cellulose was found to be an inducer of free-radical generation, a factor noted by the authors as having a probable role in the development of fibrosis (Tatrai *et al*., 1995).

Cellulose Insultation Additive Data: In addition to cellulose, chemicals with reported use in CI as flame retardants, smolder retardants or buffers were screened in the literature for relevant biological effects. A summary of these effects is presented in Table 4. The Agency for Toxic Substances and Disease Registry has prepared toxicological profiles for boron, aluminum, and ammonia which provide more complete information on some of these additives (ATSDR, 1990, 1991a,b). McConnell (1994) and Davis (1993) note that CI may also contain residuals of the paper production process as well as contaminants from various dyes, solvents and printing inks. No information was found in the published literature to verify the occurence of these compounds in CI.

Table 4. Summary of Toxicological Information on Cellulose Insulation Additives

Chemical Name [CAS RN]	Carcinogenicity Data	Genotoxicity Data	Other Related Data
Boric acid [10043-35-3]	nontumorigenic in male and female B6C3F1 mice in 2-yr feed study at 2500 or 5000 ppm (NTP, 1987) nontumorigenic in male and female Sprague-Dawley rats in 2-yr feed studies at 117, 350 or 1170 ppm (FASEB, 1980)	negative in *S. typhimurium* TA100, TA1535, TA1537, TA98 with or without S9 (NTP, 1987) negative in mouse lymphoma L5178Y/TK$^{+/-}$ with or without S9 (NTP, 1987) negative for SCEs in CHO cells with or without S9 (NTP, 1987) negative for chromosome aberrations in CHO cells with or without S9 (NTP, 1987)	eye and upper respiratory tract irritant at <10 mg/m^3 in workers exposed to dust (NLM 1995a) testicular atrophy and inter-stitial cell hyperplasia in male mice at 5000 ppm in 2-yr feed study (NTP, 1987) developmental changes in rat, mouse, and rabbit at high doses; (mouse: increased incidence of short rib and resorptions at 175 mg B/kg/day; rat: shortening of rib at 28.5 mg B/kg/day; rabbit: intraventricular septal defects, enlarged aorta and increased prenatal mortality at 43.7 mg B/kg/day) (Culver *et al*., 1995)

Borax [1303-96-4]	NDF	negative in *S. typhimurium* TA98, TA100 with or without S9 (NLM, 1995b) crude borax ore, kernite ore and refined borax were not significantly mutagenic in assays for mutation to ouabain resistance in human fibroblasts or mouse embryo fibroblasts and were weakly mutagenic in assay for 8-azaguanine resistance in Chinese hamster V-79 cells (Landolph, 1985)	workers industrially exposed to borax often suffer from chronic eczema; long-term exposure to dust may lead to inflammation of the mucous membranes of the airways and to conjunctivitis (NLM, 1995c) testicular degeneration and cessation of spermatogenesis in beagle dogs fed 1170 ppm boron as borax for 38 wk (FASEB, 1980) 2000 ppm in diet for 60 days produced total infertility in male rats for at least 32 weeks after treatment (FASEB, 1980)
Sodium metaborate [7775-19-1]	nontumorigenic in male and female Swiss mice exposed to 5 ppm in drinking water for 2 yr (FASEB, 1980)	NDF	once a tetra-, di-, meta-, ortho-, or pyroborate salt dissolves in a buffered solution, one borate cannot be distinguished on chemical or toxicological grounds from any of the others (NLM, 1995c)
Alumina trihydrate [21645-51-2]	NDF	aluminum compounds have been evaluated as non-mutagenic by most standard methods of mutagenic assays (NLM, 1995d)	essentially harmless by oral administration; on occasion workers chronically exposed to aluminum-containing dusts or fumes have developed severe pulmonary reactions including fibrosis, emphysema and pneumothorax (Gosselin *et al*., 1984)
Ammonium sulfate [7783-20-2]	no enhancement of benzo[a]pyrene-induced lung carcinogenesis in Syrian hamsters at exposures 20 times average U.S. ambient air levels (NLM, 1995e)	NDF	low toxicity (NLM, 1995e)
Gypsum [13397-24-5]	25 mg dust ip 1/wk for 4 wk to female Wistar rats resulted in 5.7% incidence of abdominal and/or thoracic tumors over lifespan; no tumors in controls (PHS-149, 1976-1977)	NDF	NDF

NDF: no data found; SCE: sister chromatid exchange; CHO: Chinese hamster ovary; ip: intraperitoneal

Structure/Activity Relationships: A brief review of fiber carcinogenicity and a summary of information relevant to the characterization of CI fibers are included in this section for assessment purposes. In addition, two organic dusts, wood dust and soft paper dust, were screened for data relevant to an assessment of CI.

Fiber Characteristics: There have been extensive studies on the carcinogenicity of mineral fibers including asbestos, glasswool, and ceramic fibers. These studies have generated the following observations on fiber characteristics and carcinogenic potential.

In occupational health, fibers are arbitrarily defined as elongated particles with a length-to-diameter ratio ≥ 3:1. The International Organization for Standardization has proposed that this ratio be increased to ≥ 5:1. Respirable fibers are defined as those with a diameter ≤3 µm and up to about 100 µm in length. For counting purposes, they have a length ≥5 µm.

Fibers ≤1.5 µm in diameter and ≥ 8µm in length are believed to be the most oncogenic when implanted into the pleural and peritoneal cavities of rats (WHO/IARC, 1983).

The precise mechanisms by which fibers exert a carcinogenic effect are unknown. Present scientific knowledge indicates that the major determinants of the carcinogenic potential of fibers are biological durability, dimensions (length and diameter), and dose to the target organ. In studies of experimental animals exposed to mineral fibers by inhalation in which significant tumor levels are seen, a high frequency of fibrosis is usually found (IARC, 1988).

The bulk of material composing CI is considered "nuisance" dust (Daniels *et al*., 1985). In contrast to fibrogenic dusts which cause scar tissue to be formed in the lungs when inhaled in excessive amounts, nuisance dusts are stated to have little adverse effect on lungs and do not produce significant organic disease or toxic effect when exposures are kept under reasonable control. The nuisance dusts have also been called biologically "inert" dusts, a term that is inappropriate to the extent that there is no dust which does not evoke some cellular response in the lung when inhaled in sufficient amount. The lung-tissue reaction caused by inhalation of nuisance dusts has the following characteristics: 1) the architecture of the air spaces remains intact, 2) collagen (scar tissue) is not formed to a significant extent, and 3) the tissue reaction is potentially reversible (ACGIH, 1991). However, the study by Tiesler and Schnitteger (1992) does indicate that there is a potential for exposure to respirable fibrous dust during the installation of CI. They reported that fiber concentrations reached upper values of approximately 50 and 30 million fibers/m^3 for fibers with diameters of < 3 and < 1 µm, respectively. Only fibers with a length-to-diameter ratio ≥3:1 were counted. Respirable dust is capable of reaching the non-ciliated, alveolar regions of the lung and may accumulate because of its size, which most often is less than 5 µm. If these dusts are toxic or irritating, tissue reaction may occur (Ferguson, 1984).

While there is little information on the effects of CI exposure, there have been studies on the adverse effects of exposures to wood dust and soft paper dust, materials likely to have a fibrous cellulose component.

Wood Dust: IARC (1995) classifies wood dust as Group 1 (carcinogenic to humans). The IARC Working Group concluded that there was "sufficient evidence" in humans for the carcinogenicity of wood dust and "inadequate" evidence in experimental animals for the carcinogenicity of wood dust. The following information is summarized from the IARC (1995) monograph on wood dust.

The essential chemical constituents of wood are cellulose (40-50%), polyoses (hemicelluloses) and lignin. In addition, a heterogeneous mixture of organic and inorganic compounds occurs in different species of wood in various amounts.

Wood dust particles are typically irregular in shape and have rough surfaces. Most of the wood dust (by mass) found in work environments has a mean aerodynamic diameter of more than 5 µm. Although no studies of the deposition of wood dust in human airways were available, it was noted that large particles (>10 µm) are almost entirely deposited in the nose. Heavy exposure to wood dust may result in decreased mucociliary clearance and, sometimes, in mucostasis.

Most of the available cohort and case-control studies of cancer of the nasal cavities and paranasal sinuses have shown increased risks associated with exposure to wood dust. Very high relative risks for adenocarcinoma at this site, associated with exposure to wood dust, have been observed in many countries.

In view of the overall lack of consistent findings, there is no indication that occupational exposure to wood dust has a causal role in cancers of the oropharynx, hypopharynx, lung, lymphatic and hematopoietic systems, stomach, colon or rectum.

Impaired respiratory function and increased prevalences of pulmonary symptoms and asthma occur in workers exposed to wood dust, especially that from western red cedar.

Soft Paper Dust: A Swedish team has published several studies on the effects of worker exposure in a soft paper mill (Thoren *et al*., 1989; Ericsson *et al*., 1988; Jarvholm *et al*., 1988). The relevant findings from these studies are summarized as follows.

Soft paper is used in toilet paper, paper towelling, and napkins. In the production of soft paper, papermaking pulp and waste paper are used in varying amounts. The increasing use of waste paper, about 80%, has made the production process dustier because the fibers in waste paper are shorter and they loosen from the web more easily. There was additional exposure mainly to the various additives used, but the contribution by weight of these additives was low, usually in the range of 0.1% (Jarvholm *et al.*, 1988).

The mean concentrations of paper dust in different departments ranged from 0.1 to 14.5 mg/m^3. Preliminary measurements indicated that 10 to 15% of the particles had a diameter of less than 5 µm (Ericsson *et al*., 1988).

Persons with long-term (>10 years) and heavy exposure to dust seemed to have impaired respiratory function compared to those with low- and/or short-term exposure to such dust. Two of the exposed men underwent lung biopsies, one of which showed fibrotic alveolar walls (Jarvholm *et al*., 1988).

In a case-referent study encompassing 33 cases and 228 referents, the potential risk for asthma and chronic obstructive pulmonary disease and respiratory cancer among workers was evaluated. There was no significantly increased risk for respiratory cancer among the exposed men. The study did suggest an excess mortality from asthma and chronic obstructive pulmonary disease among workers in a soft paper mill (Thoren *et al*., 1989).

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